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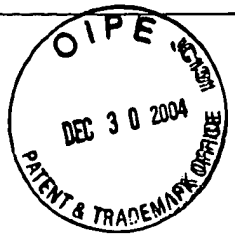

In re Application of:

JONES, et al.

Serial No.: 09/828,276

Filed: April 5, 2001

Art Unit: 1623

Examiner: D. Khare

Atty. Docket No.: 00-721-US

ADENOSINE CYCLIC KETALS: NOVEL ADENOSINE ANALOGUES FOR PHARMACOTHERAPY

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Dear Sir:

Submitted herewith are sheets of formal drawings, Figures 1-6B, Sheets 1-7, for filing in connection with the above-identified application. Each sheet of drawing has the identifying indicia suggested in 37 CFR §1.84(c) on the reverse side of the drawing.

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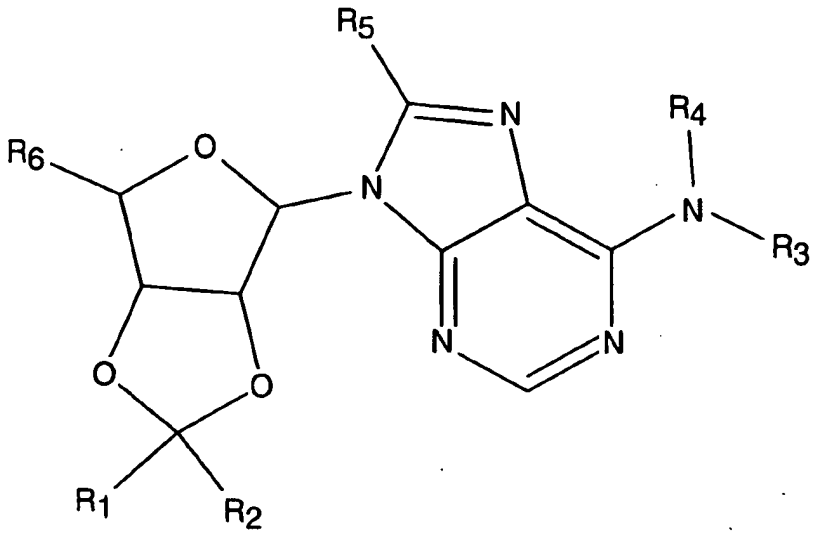
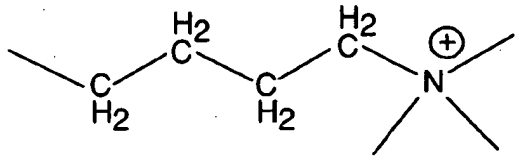
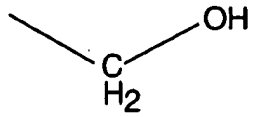


ADENOSINE CYCLIC KETAL (ACK)

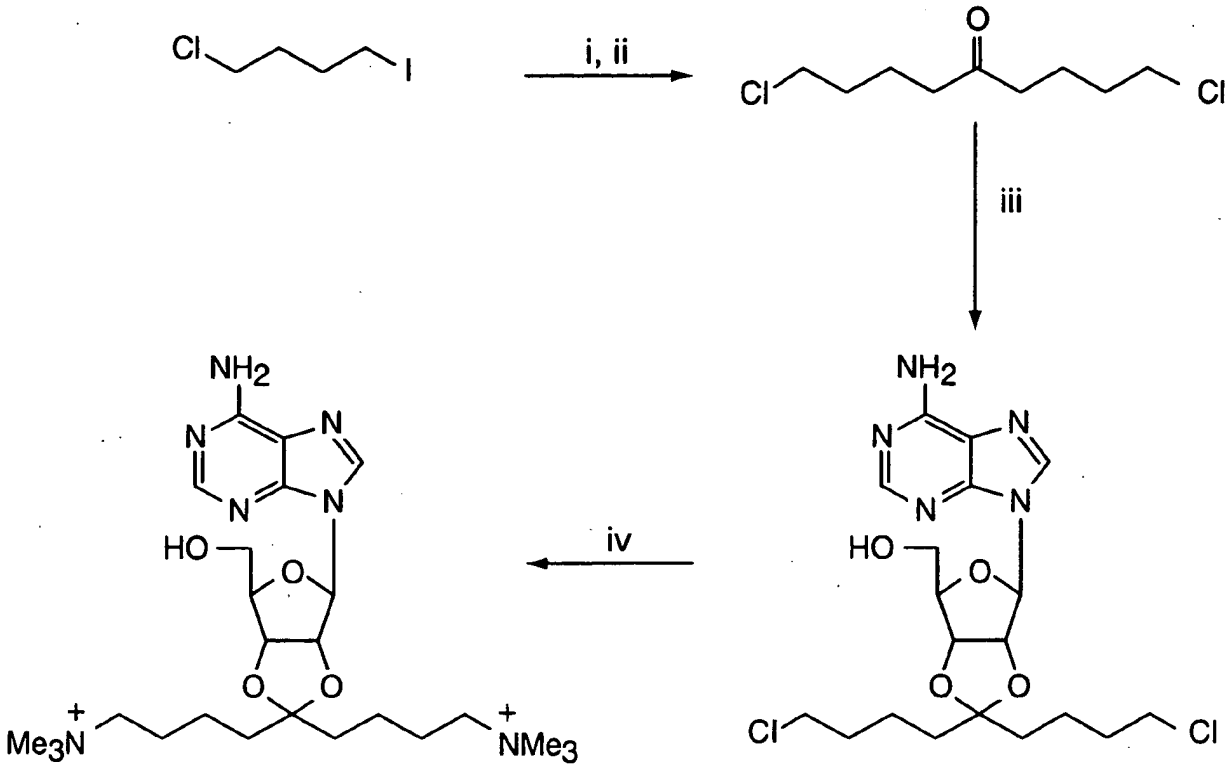
WHEN $R_1 = R_2 =$ 

AND R_3, R_4 AND R_5 = HYDROGEN

AND $R_6 =$ 

CHEMICAL STRUCTURE OF ADENOSINE CYCLIC KETAL (ACK) AND THE CHEMICAL FORMULA OF THE COMPOUND NONAMETHONIUM ADENOSINE CYCLIC KETAL (NONAMETHONIUM ACK).

FIG. 1A



The synthetic scheme for synthesizing nonamethonium adenosine cyclic ketal. The reagents and conditions are: i) zinc dust, tetrahydrofuran (THF); ii) N-methylpyrrolodine, $CoBr_2$, carbon monoxide; iii) adenosine, HCl/dioxane, $(EtO)_3CH$, DMF; iv) 40% Me_3N in H_2O.

FIG. 1B

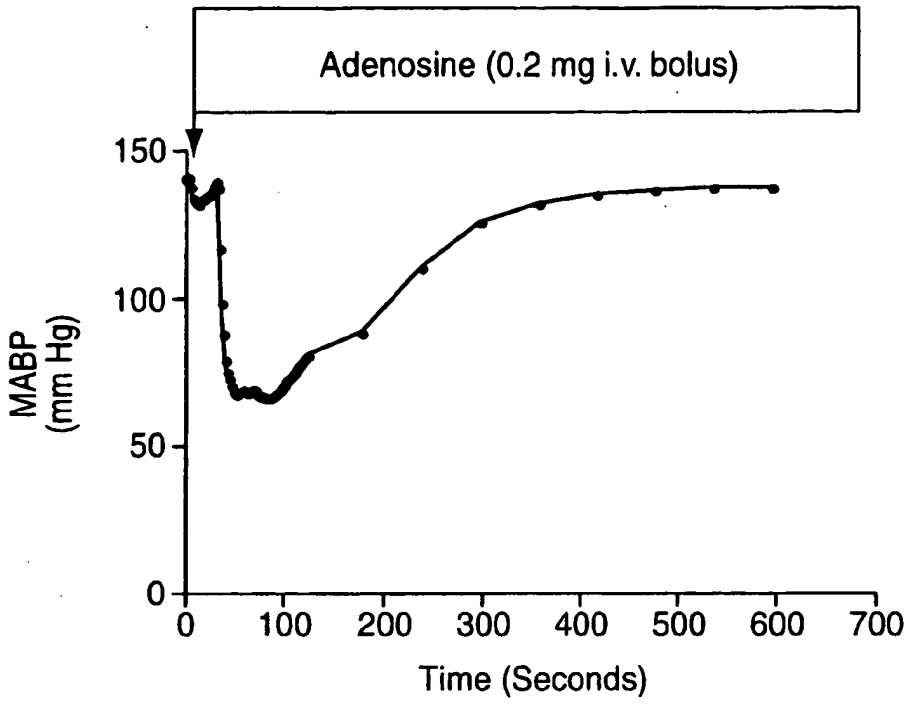

Adenosine (0.2 mg i.v. bolus)
MABP (mm Hg)
150
100
50
0
0
100
200
300
400
500
600
700
Time (Seconds)

FIG. 2A

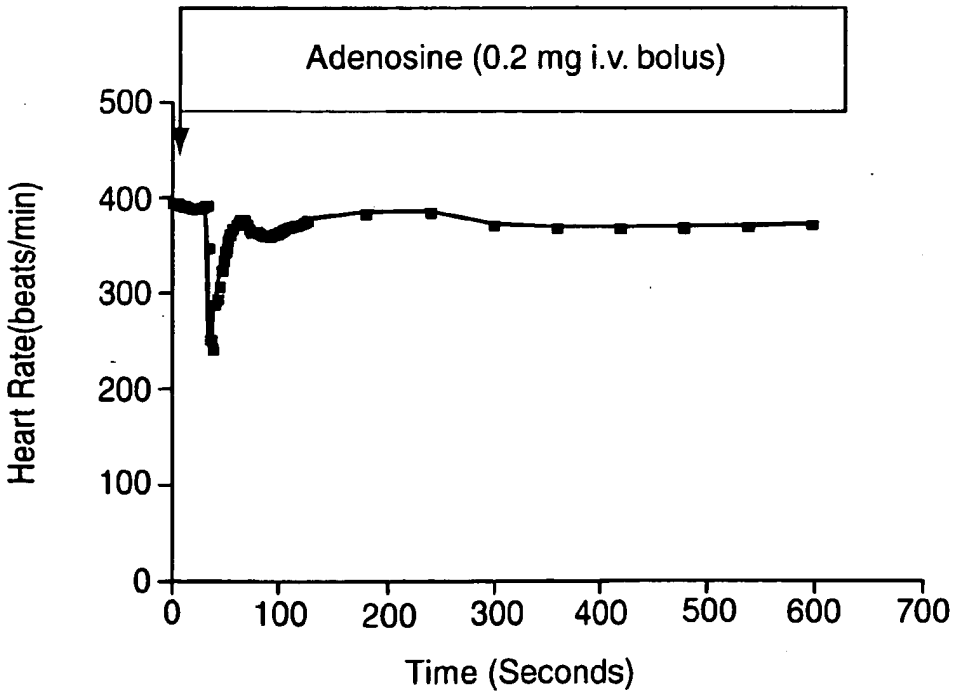

Adenosine (0.2 mg i.v. bolus)
Heart Rate(beats/min)
500
400
300
200
100
0
0
100
200
300
400
500
600
700
Time (Seconds)

FIG. 2B

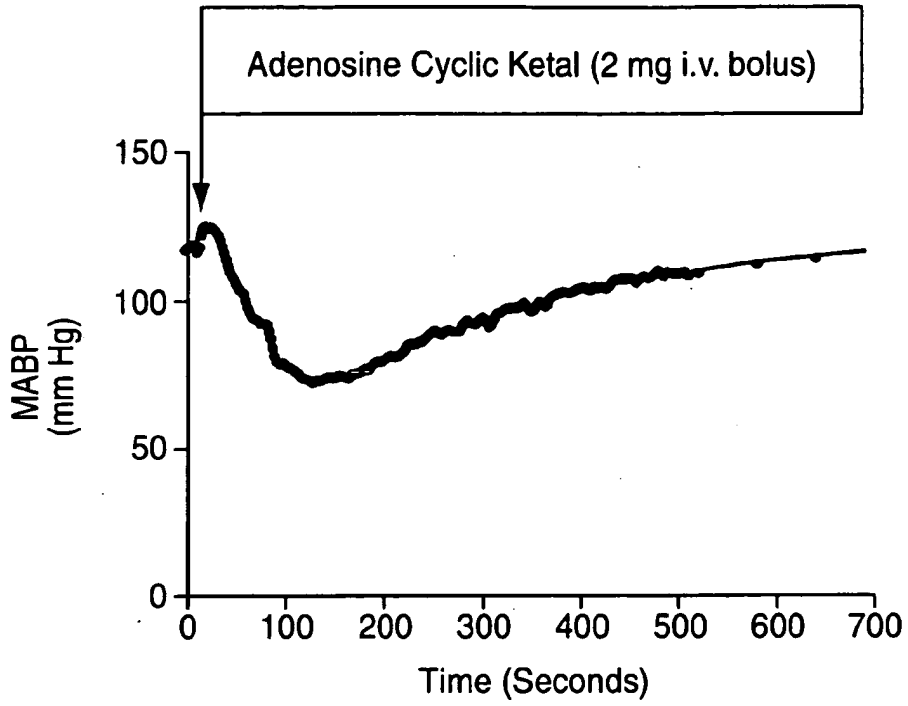

Adenosine Cyclic Ketal (2 mg i.v. bolus)
MABP (mm Hg)
150
100
50
0
0
100
200
300
400
500
600
700
Time (Seconds)

FIG. 3A

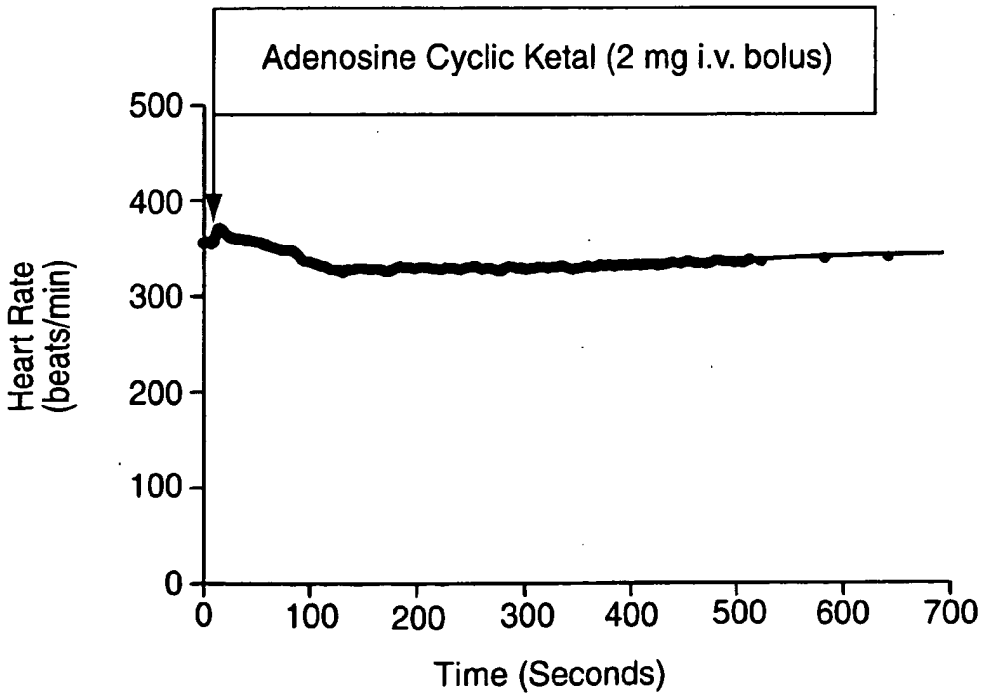

Adenosine Cyclic Ketal (2 mg i.v. bolus)
Heart Rate (beats/min)
500
400
300
200
100
0
0
100
200
300
400
500
600
700
Time (Seconds)

FIG. 3B

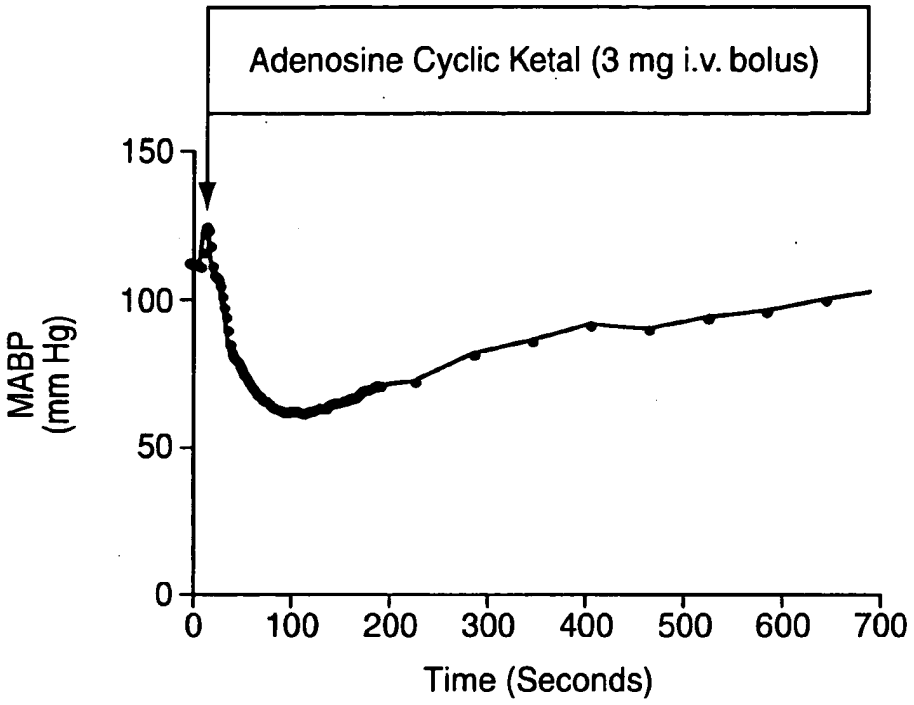

Adenosine Cyclic Ketal (3 mg i.v. bolus)
MABP (mm Hg)
150
100
50
0
0
100
200
300
400
500
600
700
Time (Seconds)

FIG. 4A

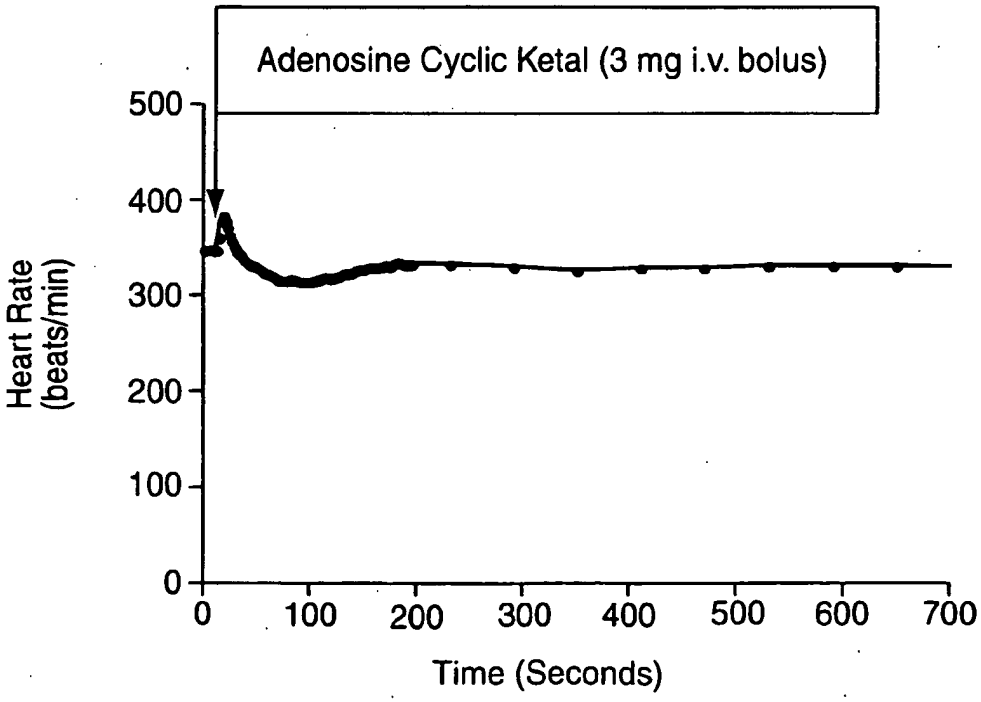

Adenosine Cyclic Ketal (3 mg i.v. bolus)
Heart Rate (beats/min)
500
400
300
200
100
0
0
100
200
300
400
500
600
700
Time (Seconds)

FIG. 4B

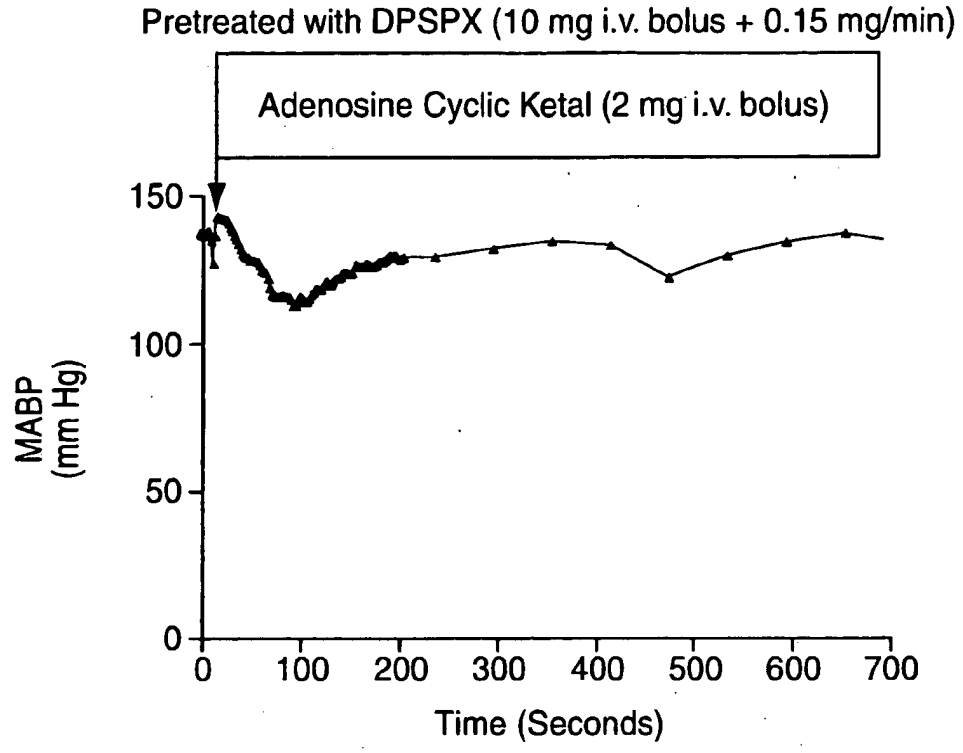

Pretreated with DPSPX (10 mg i.v. bolus + 0.15 mg/min)
Adenosine Cyclic Ketal (2 mg i.v. bolus)
MABP (mm Hg)
150
100
50
0
0
100
200
300
400
500
600
700
Time (Seconds)

FIG. 5A

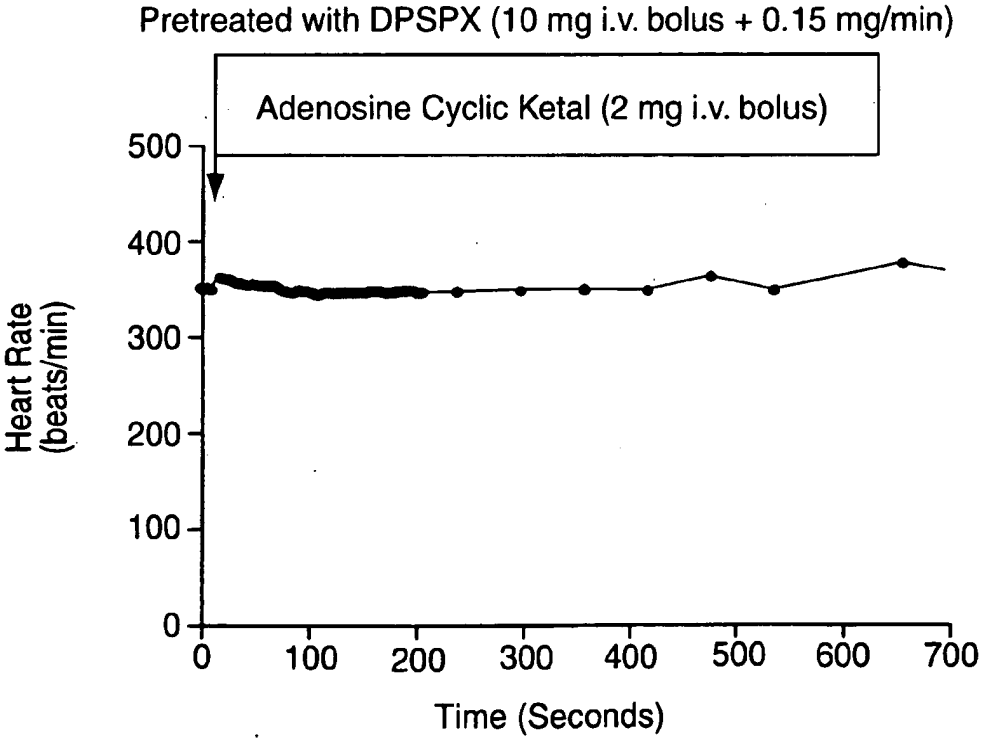

Pretreated with DPSPX (10 mg i.v. bolus + 0.15 mg/min)
Adenosine Cyclic Ketal (2 mg i.v. bolus)
Heart Rate (beats/min)
500
400
300
200
100
0
0
100
200
300
400
500
600
700
Time (Seconds)

FIG. 5B

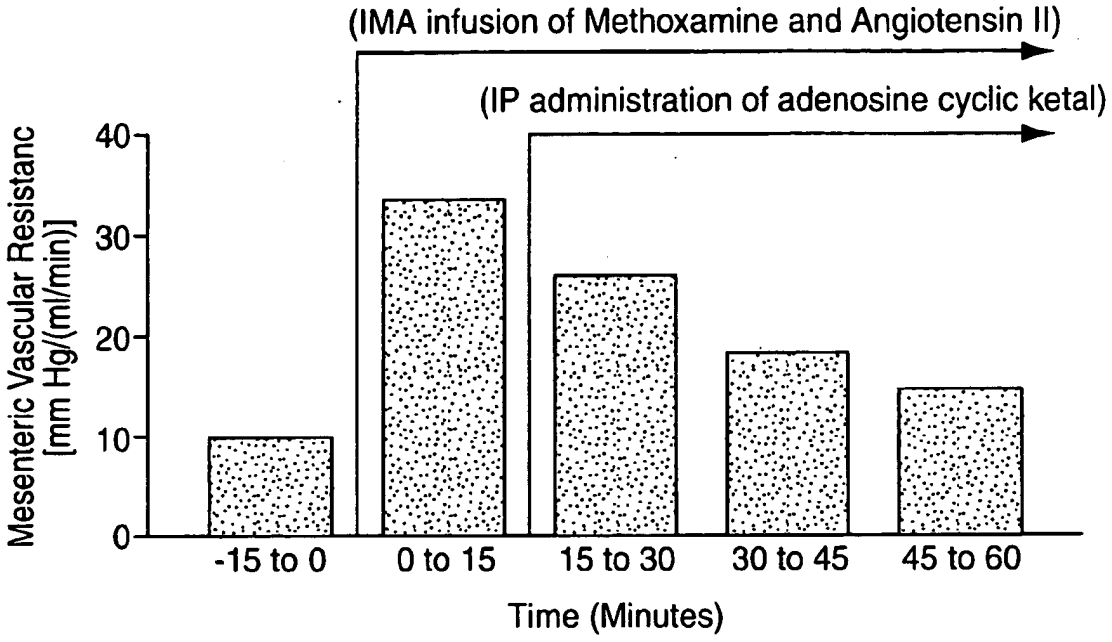

(IMA infusion of Methoxamine and Angiotensin II)
(IP administration of adenosine cyclic ketal)
Mesenteric Vascular Resistanc
[mm Hg/(ml/min)]
40
30
20
10
0
-15 to 0
0 to 15
15 to 30
30 to 45
45 to 60
Time (Minutes)

FIG. 6A

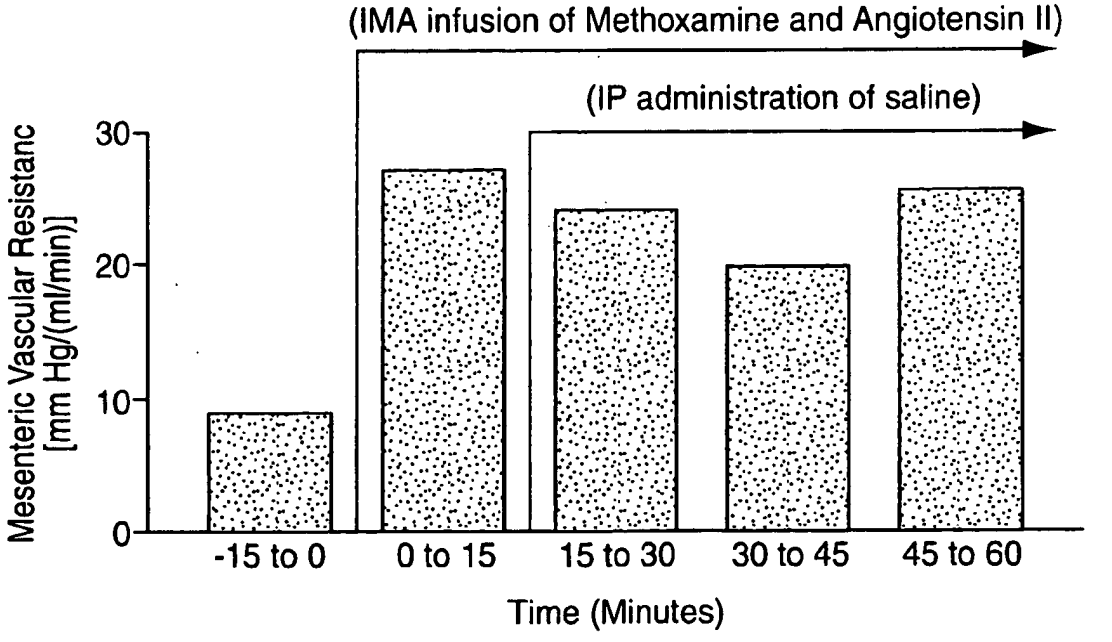

(IMA infusion of Methoxamine and Angiotensin II)
(IP administration of saline)
Mesenteric Vascular Resistanc
[mm Hg/(ml/min)]
30
20
10
0
-15 to 0
0 to 15
15 to 30
30 to 45
45 to 60
Time (Minutes)

FIG. 6B